REMARKS

In the Office Action dated December 8, 2009, claims 1-62 were pending. The Examiner has made the Restriction Requirement final. Consequently, claims 47-62 were withdrawn from further consideration. Claims 1-46 were examined and were rejected or objected to.

This Response addresses each of the Examiner's rejections and objections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Amendments to Specification and Claims

The specification, including the title and the abstract, has been amended as indicated hereinabove, to address formality issues. No new matter is introduced.

The claims have been amended to more clearly define certain specific embodiments of the invention. For example, claim 1 has been amended to include features delineated previously in dependent claims 2, 3, 6 and 10. Claims 2-3, 5-6 and 10 have therefore been canceled in view of the amendments to claim 1. Applicants reserve the rights to pursue the subject matter of the canceled claims in a continuation and/or divisional application. No new matter is introduced by the foregoing amendments to the claims.

Formality Objections

The abstract, the title and the disclosure are objected to for various informalities. It is respectfully submitted that the foregoing amendments have fully addressed the objections.

Claims 5-11, 16-27 and 32-43 are objected to under 37 CFR §1.75(c) as improper multiple dependent claims. Therefore, these claims have not been treated on the merits. It is

respectfully submitted that the claims, as presently amended, do not contain improper multiple dependent claims.

Claims 3, 14 and 30 are objected to because the phrase "retroviral viral" is redundant. Claim 3 has been amended to delete the term "viral". Claims 14 and 30 are among the canceled claims.

In view of the foregoing, it is respectfully submitted that the formality objections to the disclosure and the claims are overcome. Withdrawal of the formality objections is therefore respectfully requested.

Nonstatutory Obviousness-Type Double Patenting

Claims 1-4, 12-15, and 28-31 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claim 3 of U.S. Patent No. 7,276,242 B1 in view of Rosenwirth *et al.* (*J. Medical Primatology* 28: 195-205, 1999) ("Rosenwirth").

According to the Examiner, the patent claim differs from the instant claims in that it does not specifically recite "in conjunction with interrupted anti-retroviral drug therapy". However, the Examiner contends that Rosenwirth discloses therapeutic vaccination in conjunction with stopped or interrupted anti-retroviral drug therapy, and provides the motivation that reduction of viral load by drug treatment is expected to allow the immune system to recover and to respond appropriately to the vaccine, so that the induced immune response may be capable of suppressing virus replication to such an extent that low steady-state levels of virus load can be maintained after drug treatment is stopped. Therefore, the Examiner contends that it would have been obvious to modify the method of claim 3 of the '242 patent by combining the immunization as claimed therein with a stopped anti-retroviral drug treatment.

In response, Applicants respectfully submit that the claims, as presently recited, are patentably distinct from claim 3 of the '242 patent in view of Rosenwirth.

Applicants observe that the '242 patent is directed *inter alia* to a recombinant viral construct comprising a fowlpox virus vector encoding HIV *gag* and/or *pol* and interferon-γ. Claim 3 is directed to a method of inducing, enhancing or otherwise stimulating an immune response to HIV comprising administering the viral construct. The method is proposed to alleviate AIDS symptoms and to reduce serum viral loads (column 10, line 30 *et seq.*). As disclosed in the '242 patent, the construct may be co-administered with a known antiviral compound or molecule. Co-administration is defined (see column 11, line 15 *et seq.*) as simultaneous or sequential administration including a time difference of seconds, minutes, hours or days between administration of the vaccine and the known antiviral compound which may be administered in any order.

Applicants respectfully submit that the '242 patent does *not* address the problem to which the present invention is directed, that of reducing or delaying retroviral rebound in HIV infected subjects after interrupting anti-retroviral drug therapy. It could not have been reasonably expected from claim 3 of the '242 patent or Rosenwirth, or the combination of both, whether or not the subject viral construct would affect viral rebound after interruption of anti-retroviral drug treatment.

Rosenwirth describes anti-retroviral drug therapy and the problems associated with viral rebound upon interruption of therapy. The hypothesis that combined drug therapy and therapeutic vaccination would reduce or delay viral rebound after stopping drug therapy was not identified by Rosenwirth. Rosenwirth tested the hypothesis in a non-human primate model and found no evidence of a reduction or delay in viral rebound as a result of therapeutic vaccination

(see Figure 1 on page 198 of Rosenwirth). Rosenwirth report that one of two vaccinated Rhesus macaques showed a reduction in viral load after cessation of therapy, while the other macaque exhibited greater viral levels after stopping chemotherapy. One of two control animals receiving PMPA drug therapy alone, showed rebound followed by a reduction in viral load. Therefore, Applicants respectfully submit that these results in Rosenwirth are inconclusive, given the lack of statistical significance associated with the results together with the absence of any other supporting evidence.

Applicants also provide a copy of Markowitz *et al.*, *Journal of Infectious Diseases*, *186*: 634-643, 2002 (hereinafter referred to as "Markowitz") (copy *attached*), which reflects the state of the art at the priority date of the present invention. The studies reported by Markowitz were also disclosed by Ho *et al.*, as discussed below. Markowitz discloses another attempt to prevent viral rebound after cessation of retroviral drug therapy by administering ALVACvcp1452 and recombinant gp160 to HIV infected subjects. Despite prolonged drug therapy and apparent suppression of viral replication with or without adjunctive therapeutic vaccination, all subjects experienced virus rebound when treatment was discontinued. Virus rebound was followed by spontaneous but transient reduction in viral load, suggesting that further investigations were warranted.

Applicants respectfully submit that while the prior art may have provided an invitation to experiment, the art provided no indication that such experimentation would arrived at the present invention, nor any indication of which therapeutic vaccine might be effective.

Contrasting the failures reported in the art, the present specification provides the significant results of a clinical trial in humans showing that a pox virus vector encoding *gag* and/or *pol* and interferon-γ can reduce or delay viral rebound during interruption of anti-retroviral

drug treatment. See pages 41-43 of the specification, for example, where a "10 fold reduction in average viral fold" was observed despite of "the lack of any demonstrable immune response in the early part of the trial" (page 43, lines 22-25). Applicants respectfully submit that these results achieved by the present invention were entirely unexpected.

Applicants have amended the claims to more clearly define the invention supported by the unexpected results. It is respectfully submitted that the claims, as amended, are not obvious in view of claim 3 of the '242 patent and Rosenwirth. Withdrawal of the non-statutory double patenting rejection is therefore respectfully requested.

35 U.S.C. §112, Second Paragraph

Claims 1-4, 12-15, 28-31 and 44-46 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

Claim 2, allegedly lacking antecedent basis for certain recitation, has been canceled without prejudice, rendering the rejection thereof moot.

The term "low retroviral load" in claims 1, 3, 4, 12, 14, 15, 30 and 31 is objected to as indefinite. The Examiner alleges that the term "low" is not defined by the claim, and the specification does not provide a standard for ascertaining the requisite degree.

To the contrary, the phrase "low retroviral load" is defined in the specification, e.g., on page 32, lines 21-28. Applicants respectfully submit that those skilled in the art would clearly understand the phrase in light of the disclosure in the specification.

Regarding claims 1, 12 and 28, the Examiner maintains that it is not readily apparent as to how the administration of a poxvirus vector encoding a retroviral antigen will reduce or alleviate "one or more side effects of anti-retroviral drug therapy" as recited in the preamble. The

Examiner has proposed to replace the language "reducing or alleviating one or more side effects of anti-retroviral drug therapy" in the preamble, with the phrase "reducing or delaying viral rebound during interruption of anti-retroviral drug treatment".

In response, claim 1 has been amended to adopt the Examiner's suggestion. Claims 12 and 28 have been canceled, without prejudice.

Claims 44-46 are also rejected as indefinite because the claims provide for the use of a recombinant vector, but do not set forth any steps involved in the process.

Applicants have canceled claims 44-46 without prejudice.

In view of the foregoing, Applicants respectfully submit that the claims, as amended, are not indefinite. Withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

35 U.S.C. §101

Claims 44-46 are rejected under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter.

The rejection is rendered moot in view of the cancellation of these claims, and withdrawal thereof is respectfully requested.

35 U.S.C. §112, First Paragraph

Claims 1-4, 12-15 and 28-31 are rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. The rejection is directed to the genus of functional homologs, derivatives, part or analogs of retrovirus antigens and/or cytokines that are required to maintain or prolong a low retroviral load in a subject.

Applicants respectfully submit that references to "functional homologs, derivatives,

parts or analogs" have been deleted from the claims.

Claims 1-4 and 12-15 are rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the enablement requirement.

The Examiner is taking the position that the specification does not reasonably provide enablement for *preventing* viral rebound during interruption of anti-retroviral drug treatment. Additionally, the Examiner contends that the specification does not provide enablement for the use of a poxvirus vector encoding a homolog, analog, part or derivative of a retrovirus antigen and/or cytokine.

Applicants have amended the claims to delete the term "preventing" and references to "functional homologs, derivatives, parts or analogs".

In view of the foregoing, Applicants respectfully submit that the rejections under 35 U.S.C. §112, first paragraph, have been overcome, and withdrawal thereof is respectfully requested.

Prior Art Rejections

Claims 1-4 are rejected under 35 U.S.C. §102(b) as anticipated by Ho *et al.* (WO 01/54701 A1).

The studies reported by Markowitz were also described by Ho *et al.* Markowitz reported that there was no difference detected in virus rebound rates in subjects vaccinated with ALVACvcp1452 and recombinant gp160 *versus* subjects treated with anti-viral therapy alone. Further, there was no correlation between immunogenicity and viral control during treatment interruption.

Ho *et al.* describe (see page 33) subjects 1309 and 1306 who exhibited a delayed

rebound and lower post-rebound HIV RNA levels. Figure 5 illustrates results showing delayed rebound in subjects 1309 and 1306, but not in subjects 1310 and 1308. However, as reported in Markowitz, these results were not statistically significant. In the context of an art replete with failure, these reports merely indicate ongoing experimentation, but neither provides any guidance regarding which treatment regime or which therapeutic vaccine would be effective in controlling viral rebound. Ho *et al.* suggest combining an HIV antigen with an immunostimulatory or co-stimulatory molecule such as interleukin 2, but do not suggest co-expression, much less co-expression with interferon-γ.

A rejection of a claim under 35 U.S.C. §102(b) requires that the single prior art reference disclose every element of the claim. The absence from the reference of any claimed element negates anticipation. Kloster Speedsteel AB v Crucible Inc., 793 F.2d 1565, 1571, 230 USPQ 81, 84 (Fed. Cir. 1986). Thus, Ho *et al.* fail to anticipate the invention, as presently claimed. The rejection under 35 U.S.C. §102(b) based on Ho *et al.* has been overcome.

Claims 12-15 and 28-31 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Ho *et al.* (WO 01/54701) in view of Kent *et al.* (WO 00/28003).

Kent *et al.* disclose a fowl pox viral vector encoding HIV Gag and/or Pol and interferon-γ that is effective in stimulating an immune response to HIV Gag and/or Pol. The Examiner appears to consider that it would have been obvious to substitute the vector of Ho *et al.* with that of Kent *et al.* with a reasonable expectation that the vector would reduce or delay viral rebound.

However, Applicants respectfully submit that the ability of the subject vector to reduce or delay viral rebound, particularly in the absence of a detected immune response, would not have been predictable. In this regard, the Examiner's attention is directed to the results of a

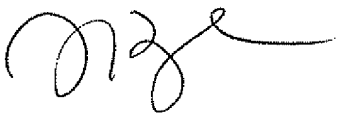
clinical trial in humans described in the specification, showing that a pox virus vector encoding *gag* and/or *pol* and interferon-γ achieved a "10 fold reduction in average viral fold" was observed despite of "the lack of any demonstrable immune response in the early part of the trial" (page 43, lines 22-25). Similarly, the ability of the full construct (encoding interferon-γ) and not the partial construct (not encoding interferon-γ) to delay or reduce viral rebound would have been similarly unpredicatable from the prior art. Applicants respectfully submit that without an understanding of what controls viral rebound in subjects undergoing drug treatment interruption, there would have been no obvious reason to select the vector of Kent *et al.* from the plurality of putative immunotherapeutic vaccines available in the art, and to substitute such selected vector for that disclosed in Ho *et al.*

Therefore, it is respectfully submitted that the claims, as amended, are not obvious in view of the combination of Ho *et al.* and Kent *et al.* Withdrawal of the rejection under 35 U.S.C. §103(a) based on the combination of Ho *et al.* and Kent *et al.* is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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